benign bladder, ureteral or cortical tissues (chi-square test, $p = 0.0073$). There is a moderate correlation for urine 3-HAA measurement based on between HPLC and the biosensor assays ($r^2 = 0.47$, $p = 0.0033$). Besides, the 3-HAA content within the cultured media of TCCSUP and BFTC905 measured with biosensors significantly increased with incubation time ($p < 0.0001$). Finally, Patients with urothelial carcinoma of bladder and upper tract have higher urine 3-HAA levels than those without recurrence or benign urological disease, such as BPH, or hernia (unpaired t-test, $p = 0.028$), except for urolithiasis.

Conclusion: The integrated biosensor exhibited a modest accuracy in urine 3-HAA detection. Both of urothelial carcinoma of urinary bladder and upper tract exhibited higher IDO expression and its metabolite 3-HAA in urine.

MP5-5.
CERAMIDE PROMOTES TNF-α-INDUCED CELL DEATH VIA DECREASING AKT ACTIVITY IN BLADDER CANCER CELL

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Purpose: Bladder cancer, a malignant urinary system tumor, is in the ninth position of the international cancer charts. The cancer shows a highly recurrent rate that is around 50%~60%. Therefore, investigating a new therapy to improve the curing rate of the cancer is important. Nowadays, Bacillus- Calmette-Guerin (BCG) immune therapy is the most common way for the treatment of bladder cancer. However, there are around 20 % patients unable to get any benefit from this, and the main mechanism of the effect of BCG is still unclear. Since BCG treatment have reported, that macrophages might be recruited into the bladder to induce cancer cell death by the pro-inflammatory response, we further study the mechanism of BCG. We used lipopolysaccharide to induce macrophage Raw264.7 for the generation of condition medium (CM-LPS). Our results demonstrated that CM-LPS might cause cell death via a caspase-dependent manner in MBT2 bladder cancer cells. As compared with CM-LPS, TNF-α involved the cell death. Moreover, TNF-α-induced AKT activation was found in MBT2 cell, implying that the activating AKT may have anti-apoptotic activity. Since ceramide is generated after inflammation, we propose that ceramide may increase TNF-α-induced cell death in bladder cancer.

Materials and methods: MBT-2 cell were treated with different concentrations of TNF-α, ceramide, and then the cell death were analyzed with MTS analysis and Hoechst3334.2 staining for chromatin condensation. The mechanisms of the cell death of TNF-α combining with ceramide were investigated by using western blotting to detect AKT activation.

Results: In our study exhibits that TNF-α had slightly to induce MBT2 cell death. Moreover, using western blot to analyze AKT expression in bladder cell were exhibited that ceramide decrease AKT activation. In our study, ceramide reduced AKT activity, promoted mitochondrial disruption and dephosphorylated Bad, a BH3 containing pro-apoptotic protein. TNF-α combining with ceramide exhibited chromatin condensation and DNA fragmentation by Hochest33342 staining assay. Our findings suggest that CM-LPS has the cytotoxic activity via ceramide and TNF-α to elicit cell death in MBT2 cell.

Conclusions: In this study, we suggest that ceramide were promoted TNF-α-induced cell death via decreasing AKT activity in bladder cancer cell. These results are demonstrated that ceramide-mediated AKT inactivation may play an important role in BCG–induced cell death in MBT2 bladder cancer cells. Our findings suggest that improvement of bladder cancer therapy will be able to decrease the activation of AKT.

MP5-6.
TARGETED THERAPY FOR METASTATIC RENAL CELL CARCINOMA: CASE SERIES STUDY IN SINGLE HOSPITAL EXPERIENCE

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Purpose: Treatment for metastatic renal cell carcinoma (mRCC) has recently focused on targeted therapy including tyrosine kinase inhibitors and mTOR inhibitors. Molecular-targeted therapies have been proved to be effective treatment options. We herein report the outcomes of targeted therapy for mRCC in our institution.

Materials and methods: From 2010 to 2015, 15 mRCC patients were identified in our institute under targeted therapy with a diagnosis of mRCC. Three targeted agents, namely temsirolimus, sunitinib, and everolimus, were given for patient according to the clinical condition. Sunitinib and Temsirolimus were served as first-line treatment and Everolimus was the second–line treatment. Demographics, the interval between diagnosis of metastasis and targeted therapy, the duration of targeted therapy, side effects and complications after treatment were collected with a retrospective medical record review. Response rate were analyzed according to RECIST criteria.

Results: Among the 15 patients, 9 were male and 6 were female. The mean age was 70.3 (35-88) years old. Lung metastasis was noted in 80% (12/15) of the patient, and other sites of metastasis were also noted, including lymphnodes, liver, bone and adrenal gland. The mean interval between diagnosis of metastasis and targeted therapy is 27.5 (1–78) days. The mean duration of targeted therapy is 268.5 days with temsirolimus, 397.8 days with sunitinib and 360.3 days with everolimus. The most common side effect noted in targeted therapy is anemia (100%) in temsirolimus group, hand-foot mouth syndrome (61.5%) and hypertension (61.5%) in sunitinib group, and cough (50%) (without radiologic sign of interstitial pneumonitis) in everolimus group. There were 2 patients (2/4) with disease regression and 2 (2/4) with stationary disease under everolimus usage, compared with 2 patients (2/12) with disease regression, 5 patients (5/12) with progression disease and 5 patients in stationary status under sunitinib usage. One patient with temsirolimus usage was in disease progression, and the other was in stationary status.

Conclusion: Targeted therapy prolonged the life of mRCC patients with tolerable outcome. In our series, the response rate of Everolimus is higher than expected.

MP5-7.
NEPHRON-SPARING MANAGEMENT (DISTAL URETERECTOMY WITH REIMPLANTATION OF URETER) FOR CARCINOMA OF DISTAL URETER: A SINGLE CENTER EXPERIENCE

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Purpose: Radical nephroureterectomy (NU) with bladder-cuff excision has been the traditional treatment for UTUC because of its high rate of recurrence. However, given the morbidity of nephrectomy and the risk of developing chronic kidney disease (CKD) or dialysis-dependent renal failure, a nephron-sparing approach may be preferable in selected patients.

Materials and methods: We retrospectively analyzed 19 patients from March 2006 to December 2014 at single center in Southern Taiwan who underwent distal ureterectomy with reimplantation of ureter and confirmed to be ureter malignancy (urothelial carcinoma n = 18, squamous cell carcinoma n = 1) on final pathology. Outcome measures were recurrence or distant metastasis, renal function preservation, time to recurrence and overall survival.

Results: Total 19 patients, 13 males, 6 females, and mean age are 69.3 years old. There are no local recurrence, 9 bladder recurrence (47.4%), 3 distant metastasis (15.8%), and 2 progression to radical nephroureterectomy (10.5%). Pathological staging: Tis n = 1, Ta n = 3, T1 n = 2, T2 n = 6, T3 n = 5. Low grade n = 3, high grade n = 12. Mean time to recurrence was 12.4 (3–24) months, and mean follow up time was 28.1 (1–90) months. Overall survival rate is 73.7% (14/19), among them, 4 lost follow up, 1 expired. Mean pre-op creatinine was 1.61 mg/dl, 1 yr post operation creatinine was 1.56mg/dl.

Conclusion: Distal ureterectomy with reimplantation surgery in our experience is a feasible option for distal ureter tumor in selected patients (chronic kidney disease, solitary kidney). Favorable post-operative

outcomes with low local recurrence rate, low rate of progression to NU and renal function preservation are the benefits.

MP5-8.
HISTONE DEACETYLASE INHIBITOR TRICHOSTATIN A SYNERGISTICALLY RESENSITIZES A GEMCITABINE RESISTANT UROTHELIAL CARCINOMA CELLS VIA SUPPRESSION OF TG-INTERACTING FACTOR AND AKT ACTIVATION

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Purpose: Gemcitabine and cisplatin (GC) has been widely used for advanced and metastatic urothelial carcinoma (UC). However, resistance to this remedy has been noticed. We have demonstrated that increase of TG-interacting factor (TGIF) in specimens is associated with worse prognosis of upper tract UC (UTUC) patients. The roles of TGIF in the gemcitabine resistance of UTUC and a promising therapeutic strategy to UC were explored.
Materials and methods: Specimens of 23 UTUC patients who received GC systemic chemotherapy were collected to evaluate the alterations of TGIF in the resistance to the remedy by using immunohistochemistry. *In vitro* characterizations of mechanisms mediating TGIF in gemcitabine resistance were conducted by analyzing NTUB1 cells and their gemcitabine-resistant sublines, NGR cells.
Results and conclusions: Increased TGIF and p-AKT^{Ser473} are significantly associated with chemo-resistance, poor progression-free survival, and higher cancer-related deaths of UTUC patients. Higher increases of TGIF, p-AKT^{Ser473}, and invasive ability were demonstrated in NGR cells. Overexpression of TGIF in NTUB1 cells upregulated p-AKT^{Ser473} activation, migration ability, and attenuated cellular sensitivity to gemcitabine. Knockdown of TGIF in NGR cells downregulated p-AKT^{Ser473} activation, migration ability, and enhanced cellular sensitivity to gemcitabine. In addition, histone deacetylases inhibitor trichostatin A (TSA) can inhibit TGIF, p-AKT^{Ser473} expression and migration ability. Synergistic effects of gemcitabine and TSA on NGR cells were also demonstrated. Collectively, TGIF contributes to the gemcitabine resistance of UTUC via AKT activation. Combined treatment with gemcitabine and TSA might be a promising therapeutic remedy to improve the gemcitabine resistance of UC.

MP5-9.
OVEREXPRESSION OF HEPATOMA-DERIVED GROWTH FACTOR (HDGF) IS ASSOCIATED WITH WORSE PROGNOSIS IN UPPER URINARY TRACT UROTHELIAL CARCINOMA

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Purpose: Hepatoma-derived growth factor (HDGF) is a nucleus targeted growth factor, it has been reported to exert mitogenic effects on several types of cells and elevated in various types of cancers suggesting an important role in the development and progression of cancers. Our study was designed to elucidate the correlation of HDGF expression and prognosis in patients with upper urinary tract urothelial carcinoma (UTUC). The related mechanisms of HDGF involved were investigated using urothelial cancer cell lines.
Patients and methods: One hundred and fifty-eight UTUC specimens were analyzed for HDGF by immunohistochemistry. HDGF expression in urothelial cancer cell lines was analyzed by RT-PCR and western blotting. *In vitro* characterizations of the cellular function of recombinant HDGF in epithelial-mesenchymal transition (EMT) and tumorigenic behaviors were performed by trans-well assay and colony formation assay, respectively.
Results and conclusion: Overexpression of HDGF was present in 74 patients (46.8%). A positive HDGF expression was significantly associated with higher disease progression ($p = 0.036$) and cancer-related death rates ($p = 0.001$). In vitro study showed that overexpression of HDGF in non-invasive UC cells could significantly increase their cellular proliferation, colonies formation, and migration/invasion ability through the PI3K/AKT pathway. In contrast, knockdown of HDGF high expression UC cells with its specific shRNA inhibited the growth ability using colonies formation experiments. These results indicated that HDGF overexpression is associated with aggressive biological behavior of UC cells via the PI3K/AKT pathway. In conclusion, our study shown that HDGF is participated in UC disease progression processes. HDGF can be a potential prognostic prediction biomarker for patients with invasive UTUC post-operatively. Further identification of the molecular mechanisms involved and searching for specific targets related are warranted.

MP5-10.
LONG TERM RENAL FUNCTION FOLLOWING NEPHROURETERECTOMY IN UPPER URINARY TRACT TRANSITIONAL CELL CARCINOMA: 3 YEARS EXPERIENCE

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Purpose: This study is designed to evaluate the estimated glomerular filtration rate (eGFR) changes in patients undergoing radical nephro-ureterectomy (RNU) for upper tract urothelial carcinoma (UTUC).
Materials and methods: We retrospectively reviewed our patients with upper urinary tract TCC undergone nephroureterectomy from 2007 to 2012. Only patients with upper urinary tract transitional cell carcinoma (TCC) were enrolled in our study. We exclused the patients with end-stage-renal disease. Total 72 patients had completed follow up for three years after nephroureterectomy. The estimated glomerular filtration rate (eGFR) was calculated using the modified glomerular filtration rate estimating equation: eGFR (mL/min/1.73 m^2) = $175 \times \text{Scr}^{-1.234} \times \text{age}^{-0.179}$ ($\times$ 0.79 if female). We compared eGFR before surgery and one year after surgery, two years after surgery, and three years after surgery.
Results: Overall 72 patients were included in the study. The median age at surgery was 66.46 (46–86) years. 31 patients (44%) had a preoperative eGFR ≧ 60 mL/min per 1.73 m^2 and 53 (75%) had an eGFR ≧ 45 mL/min per 1.73 m^2. The preoperative CKD stage distribution was: CKD I ($n = 4$, 5.5%), CKD II ($n = 27$, 37.5%), CKD III ($n = 33$, 46%), and CKD IV ($n = 8$, 11.1%). After RNU, 15 patients (20.8%) had a postoperative eGFR ≧ 60 mL/min per 1.73 m^2 and 41 (56.9%) had an eGFR ≧ 45 mL/min per 1.73 m^2. The postoperative CKD stages distribution was: CKD I ($n = 1$, 1%), CKD II ($n = 14$, 19%), CKD III ($n = 46$, 64%), CKD IV ($n = 5$, 7%) and CKD V ($n = 6$, 8.3%). Comparison of preoperative and postoperative Scr levels for each patient showed a mean difference of 0.44 mg/dL ($P < 0.001$), which represents a median (IQR) increase of 27.2%. On similar analysis performed for eGFR, we found a mean difference between preoperative and postoperative eGFR of 10.8 mL/min per 1.73 m^2 ($P < 0.001$), which represents a median (IQR) decrease of 18.2 %. 3 years after RNU, 14 patients (19%) had a postoperative eGFR ≧ 60 mL/min per 1.73 m^2 and 37 (51.4%) had an eGFR ≧ 45 mL/min per 1.73 m^2. The long-term CKD stages distribution was: CKD I ($n = 0$, 0%), CKD II ($n = 14$, 19%), CKD III ($n = 38$, 53%), CKD IV ($n = 11$, 22.2%) and CKD V ($n = 9$, 12.5%). The eGFR decreased within years as 58.06, 47.28, 45.68, and 41.91 mL/min per 1.73 m^2 ($P < 0.001$).
Conclusions: TCCs located in the upper urinary tract had negative impact on the ipsilateral renal function. eGFR was relatively low and furthermore, it significantly decreased within years after RNU.

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